

APPLICATION NO.: 10/613,524

ATTY. DOCKET NO.: C1037.70042US00

INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT

FILING DATE: July 3, 2003

CONFIRMATION NO.: 4728

APPLICANT: Krieg et al.

GROUP ART UNIT: 1645

EXAMINER: Oluwatosin A. Ogunbiyi

Sheet 1 of 12

DEC 10 2008

## U.S. PATENT DOCUMENTS

| Examiner's Initials #<br>REMARKS | Cite No. | U.S. Patent Document |           | Name of Patentee or Applicant of Cited Document | Date of Publication or Issue of Cited Document<br>MM-DD-YYYY |
|----------------------------------|----------|----------------------|-----------|---|--|
|                                  |          | Number               | Kind Code |   |  |
|                                  | A156     | 4,806,463            |           | Goodchild et al.                                | 02-21-1989   |
|                                  | A157     | 5,004,810            |           | Draper  | 04-02-1991   |
|                                  | A158     | 5,166,195            |           | Ecker   | 11-24-1992   |
|                                  | A159     | 5,194,428            |           | Agrawal et al.                                  | 03-16-1993   |
|                                  | A160     | 5,264,423            |           | Cohen et al.                                    | 11-23-1993   |
|                                  | A161     | 5,276,019            |           | Cohen et al.                                    | 01-04-1994   |
|                                  | A162     | 5,416,203            |           | Letsinger                                       | 05-16-1995   |
|                                  | A163     | 5,780,448            |           | Davis   | 07-14-1998   |
|                                  | A164     | 6,589,940            | B1        | Raz et al.                                      | 07-08-2003   |
|                                  | A165     | 6,610,308            | B1        | Haensler  | 08-26-2003   |
|                                  | A166     | 6,749,856            | B1        | Berzofsky et al.                                | 06-15-2004   |
|                                  | A167     | 6,835,395            | B1        | Semple et al.                                   | 12-28-2004   |
|                                  | A168     | 6,852,705            | B2        | Audonnet et al.                                 | 02-08-2005   |
|                                  | A169     | 7,223,741            | B2        | Krieg   | 05-29-2007   |
|                                  | A170     | 7,271,156            | B2        | Krieg et al.                                    | 07-18-2007   |
|                                  | A171     | 7,303,881            | B2        | Huang et al.                                    | 12-04-2007   |
|                                  | A172     | 7,354,711            | B2        | Macfarlane                                      | 04-08-2008   |
|                                  | A173     | 7,354,909            | B2        | Klinman et al.                                  | 04-08-2008   |
|                                  | A174     | 7,402,572            | B2        | Krieg et al.                                    | 07-22-2008   |
|                                  | A175     | 7,410,975            | B2        | Lipford et al.                                  | 08-12-2008   |
|                                  | A176     | 2002-0065236         | A1        | Yew et al.                                      | 05-30-2002   |
|                                  | A177     | 2002-0142977         | A1        | Raz et al.                                      | 10-03-2002   |
|                                  | A178     | 2002-0151518         | A1        | Agrawal et al                                   | 10-17-2002   |
|                                  | A179     | 2002-0168340         | A1        | Agrawal   | 11-14-2002   |
|                                  | A180     | 2003-0032443         | A1        | Johnson et al.                                  | 02-13-2003   |
|                                  | A181     | 2003-0119773         | A1        | Raz et al.                                      | 06-26-2003   |
|                                  | A182     | 2003-0125279         | A1        | Junghans et al.                                 | 07-03-2003   |
|                                  | A183     | 2003-0129605         | A1        | Yu et al.                                       | 07-10-2003   |
|                                  | A184     | 2003-0176389         | A1        | Raz et al.                                      | 09-18-2003   |
|                                  | A185     | 2003-0212029         | A1        | Agrawal et al.                                  | 11-13-2003   |
|                                  | A186     | 2003-0225016         | A1        | Fearon et al.                                   | 12-04-2003   |
|                                  | A187     | 2003-0232443         | A1        | Bennett et al.                                  | 12-18-2003   |

EXAMINER:

DATE CONSIDERED:

<sup>#</sup> EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

|  |   |    |    |                             |                                   |
|--|---|----|----|-----------------------------|-----------------------------------|
| FORM PTO-1449/A and B (modified PTO/SB/08)               |   |    |    | APPLICATION NO.: 10/613,524 | ATTY. DOCKET NO.: C1037.70042US00 |
| <b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b> |   |    |    | FILING DATE: July 3, 2003   | CONFIRMATION NO.: 4728            |
|  |   |    |    | APPLICANT: Krieg et al.     |                                   |
| Sheet  | 2 | of | 12 | GROUP ART UNIT: 1645        | EXAMINER: Oluwatosin A. Ogunbiyi  |

|      |              |    |                  |            |
|------|--------------|----|------------------|------------|
| A188 | 2004-0006010 | A1 | Carson et al.    | 01-08-2004 |
| A189 | 2004-0006034 | A1 | Raz et al.       | 01-08-2004 |
| A190 | 2004-0092468 | A1 | Schwartz et al.  | 05-13-2004 |
| A191 | 2005-0079152 | A1 | Bot et al.       | 04-14-2005 |
| A192 | 2005-0159351 | A1 | Grate et al.     | 07-21-2005 |
| A193 | 2005-0209184 | A1 | Klinman et al.   | 09-22-2005 |
| A194 | 2006-0286070 | A1 | Hartmann et al.  | 12-21-2006 |
| A195 | 2006-0287263 | A1 | Davis et al.     | 12-21-2006 |
| A196 | 2007-0009482 | A1 | Krieg et al.     | 01-11-2007 |
| A197 | 2007-0010470 | A1 | Krieg et al.     | 01-11-2007 |
| A198 | 2007-0037767 | A1 | Bratzler et al.  | 02-15-2007 |
| A199 | 2007-0065467 | A1 | Krieg et al.     | 03-22-2007 |
| A200 | 2007-0066550 | A1 | Diener et al.    | 03-22-2007 |
| A201 | 2007-0066553 | A1 | Krieg et al.     | 03-22-2007 |
| A202 | 2007-0066554 | A1 | Krieg et al.     | 03-22-2007 |
| A203 | 2007-0078104 | A1 | Krieg et al.     | 04-05-2007 |
| A204 | 2007-0129320 | A9 | Davis et al.     | 06-07-2007 |
| A205 | 2007-0142315 | A1 | Forsbach et al.  | 06-21-2007 |
| A206 | 2007-0184465 | A1 | Wagner et al.    | 08-09-2007 |
| A207 | 2007-0202128 | A1 | Krieg et al.     | 08-30-2007 |
| A208 | 2007-0224210 | A1 | Krieg et al.     | 09-27-2007 |
| A209 | 2007-0232622 | A1 | Lipford et al.   | 10-04-2007 |
| A210 | 2008-0009455 | A9 | Krieg et al.     | 01-10-2008 |
| A211 | 2008-0026011 | A1 | Krieg et al.     | 01-31-2008 |
| A212 | 2008-0031936 | A1 | Krieg et al.     | 02-07-2008 |
| A213 | 2008-0045473 | A1 | Uhlmann et al.   | 02-21-2008 |
| A214 | 2008-0113929 | A1 | Lipford et al.   | 05-15-2008 |
| A215 | 2008-0146488 | A1 | Wettstein et al. | 06-19-2008 |
| A216 | 2008-0226649 | A1 | Schetter et al.  | 09-18-2008 |

#### FOREIGN PATENT DOCUMENTS

| Examiner's Initials # | Cite No. | Foreign Patent Document |           |              | Name of Patentee or Applicant of Cited Document | Date of Publication of Cited Document<br>MM-DD-YYYY | Translation (Y/N) |
|-----------------------|----------|-------------------------|-----------|--------------|---|---|-------------------|
|                       |          | Office/<br>Country      | Number    | Kind<br>Code |   |   |                   |
|                       | B23      | EP                      | 1 187 629 | A2           | Smithkline Beecham Biologicals, S.A.            | 10-26-2000  |                   |
|                       | B24      | WO                      | 95/03407  | A2           | Gen-Probe Incorporated                          | 02-02-1995  |                   |

|           |                  |
|-----------|------------------|
| EXAMINER: | DATE CONSIDERED: |
|-----------|------------------|

<sup>#</sup> EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

|  |  |  |  |                             |                                   |    |
|--|--|--|--|-----------------------------|-----------------------------------|----|
| FORM PTO-1449/A and B (modified PTO/SB/08)<br><b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b> |  |  |  | APPLICATION NO.: 10/613,524 | ATTY. DOCKET NO.: C1037.70042US00 |    |
|  |  |  |  | FILING DATE: July 3, 2003   | CONFIRMATION NO.: 4728            |    |
|  |  |  |  | APPLICANT: Krieg et al.     |                                   |    |
|  |  |  |  | Sheet                       | 3                                 | of |

|  |     |    |             |    |   |            |  |
|--|-----|----|-------------|----|---|------------|--|
|  | B25 | WO | 99/63975    | A2 | Biognostik Gesellschaft Fur Biomolekular Diagnostik MBH | 12-16-1999 |  |
|  | B26 | WO | 00/14217    | A3 | CpG ImmunoPharmaceuticals GmbH                          | 03-16-2000 |  |
|  | B27 | WO | 00/67023    | A1 | GpG ImmunoPharmaceuticals GmbH                          | 11-09-2000 |  |
|  | B28 | WO | 02/069369   | A2 | Coley Pharmaceutical Group, Inc.                        | 09-06-2002 |  |
|  | B29 | WO | 03/094963   | A2 | INEX Pharmaceuticals Corp.                              | 11-20-2003 |  |
|  | B30 | WO | 2004/012669 | A2 | The Government of the United States                     | 02-12-2004 |  |
|  | B31 | WO | 2004/016805 | A2 | Coley Pharmaceutical Group, Inc.                        | 02-26-2004 |  |
|  | B32 | WO | 2004/039829 | A2 | Coley Pharmaceutical Group, Ltd                         | 05-13-2004 |  |
|  | B33 | WO | 2004/087203 | A2 | Coley Pharmaceutical Group, Ltd.                        | 10-14-2004 |  |
|  | B34 | WO | 2006/080946 | A2 | Coley Pharmaceutical GmbH                               | 08-03-2006 |  |
|  | B35 | WO | 2007/031877 | A2 | Coley Pharmaceutical GmbH                               | 03-22-2007 |  |
|  | B36 | WO | 2007/038720 | A2 | Coley Pharmaceutical GmbH                               | 04-05-2007 |  |
|  | B37 | WO | 2008/030455 | A2 | Coley Pharmaceutical Group, Inc.                        | 03-13-2008 |  |
|  | B38 | WO | 2008/033432 | A2 | Coley Pharmaceutical Group, Inc.                        | 03-20-2008 |  |
|  | B39 | WO | 2008/039538 | A2 | Coley Pharmaceutical Group, Inc.                        | 04-03-2008 |  |
|  | B40 | WO | 2008/068638 | A2 | Coley Pharmaceutical GMBH                               | 06-12-2008 |  |
|  | B41 | WO | 2008/139262 | A2 | Coley Pharmaceutical GMBH                               | 11-20-2008 |  |

#### OTHER ART – NON PATENT LITERATURE DOCUMENTS

| Examiner's Initials | Cite No | Include name of the author (in CAPITAL LETTERS) title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, relevant page(s), volume-issue number(s), publisher, city and/or country where published. | Translation (Y/N) |
|---------------------|---------|---|-------------------|
|                     | C95     | Press Release, January 2007, "Coley Pharmaceutical Group Updates Hepatitis C Drug Development Strategy".  |                   |
|                     | C96     | Press Release, June 2007, "Coley Pharmaceutical Group Announces Pfizer's Discontinuation of Clinical Trials for PF-3512676 Combined with Cytotoxic Chemotherapy in Advanced Non Small Cell Lung Cancer".  |                   |
|                     | C97     | [No Author Listed] CPG10101 HCV Toll-Receptor 9 Antagonist Phase II Study Results. 57 <sup>th</sup> Annual Meeting of the American Association for the Study of Liver Diseases. October 27-31, 2006. Boston, MA. 9 pages.   |                   |
|                     | C98     | [No Author Listed] CpG 7909: PF 3512676, PF-3512676. Drugs R D. 2006;7(5):312-6.  |                   |
|                     | C99     | AGRAWAL et al., Antisense therapeutics: is it as simple as complementary base recognition? Mol Med Today. 2000 Feb;6(2):72-81.  |                   |
|                     | C100    | AGRAWAL et al., Chapter 19: Pharmacokinetics and bioavailability of antisense oligonucleotides following oral and colorectal administrations in experimental animals. 1998:525-43.  |                   |
|                     | C101    | AHLUWALIA et al., Immunostimulatory profiles from two classes of CpG ODN administered subcutaneously to healthy subjects. ICI FOCIS 2004. Poster.   |                   |
|                     | C102    | ANITESCU et al., Interleukin-10 functions in vitro and in vivo to inhibit bacterial DNA-induced secretion of interleukin-12. J Interferon Cytokine Res. 1997 Dec;17(12):781-8.  |                   |
|                     | C103    | AOKI et al., Use of cytokines in infection. Expert Opin Emerg Drugs. 2004 Nov;9(2):223-36.  |                   |

|           |                  |
|-----------|------------------|
| EXAMINER: | DATE CONSIDERED: |
|-----------|------------------|

<sup>#</sup> EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

|  |   |    |    |                             |                                   |
|--|---|----|----|-----------------------------|-----------------------------------|
| FORM PTO-1449/A and B (modified PTO/SB/08) |   |    |    | APPLICATION NO.: 10/613,524 | ATTY. DOCKET NO.: C1037.70042US00 |
|  |   |    |    | FILING DATE: July 3, 2003   | CONFIRMATION NO.: 4728            |
|  |   |    |    | APPLICANT: Krieg et al.     |                                   |
| Sheet                                      | 4 | of | 12 | GROUP ART UNIT: 1645        | EXAMINER: Oluwatosin A. Ogunbiyi  |

|      |   |  |
|------|---|--|
| C104 | AUF et al., Implication of macrophages in tumor rejection induced by CpG-oligodeoxynucleotides without antigen. <i>Clin Cancer Res.</i> 2001 Nov;7(11):3540-3.                                    |  |
| C105 | BALLAS et al., Induction of NK activity in murine and human cells by CpG motifs in oligodeoxynucleotides and bacterial DNA. <i>J Immunol.</i> 1996 Sep 1;157(5):1840-5.                           |  |
| C106 | BAUER et al., DNA activates human immune cells through a CpG sequence-dependent manner. <i>Immunology.</i> 1999 Aug;97(4):699-705.  |  |
| C107 | BAUER et al., Human TLR9 confers responsiveness to bacterial DNA via species-specific CpG motif recognition. <i>Proc Natl Acad Sci U S A.</i> 2001 Jul 31;98(16):9237-42.                         |  |
| C108 | BIBBY, Orthotopic models of cancer for preclinical drug evaluation: advantages and disadvantages. <i>Eur J Cancer.</i> 2004 Apr;40(6):852-7.  |  |
| C109 | BOGGS et al., Characterization and modulation of immune stimulation by modified oligonucleotides. <i>Antisense Nucleic Acid Drug Dev.</i> 1997 Oct;7(5):461-71.                                   |  |
| C110 | BOHN et al., Ambiguous role of interleukin-12 in <i>Yersinia enterocolitica</i> infection in susceptible and resistant mouse strains. <i>Infect Immun.</i> 1998 May;66(5):2213-20.                |  |
| C111 | CHACE et al., Bacterial DNA-induced NK cell IFN-gamma production is dependent on macrophage secretion of IL-12. <i>Clin Immunol Immunopathol.</i> 1997 Aug;84(2):185-93.                          |  |
| C112 | CONNELL et al., Anti-tumor activity of a CpG-containing oligodeoxynucleotide (ODN) in athymic mice. <i>American Assn Cancer Reseach.</i> March 1999;40:Abstract 1982.                             |  |
| C113 | COOPER et al., CPG 7909 adjuvant improves hepatitis B virus vaccine seroprotection in antiretroviral-treated HIV-infected adults. <i>AIDS.</i> 2005 Sep 23;19(14):1473-9.                         |  |
| C114 | COWDERY et al., Bacterial DNA induces NK cells to produce IFN-gamma in vivo and increases the toxicity of lipopolysaccharides. <i>J Immunol.</i> 1996 Jun 15;156(12):4570-5.                      |  |
| C115 | DAVIS, Use of CpG DNA for enhancing specific immune responses. <i>Curr Top Microbiol Immunol.</i> 2000;247:171-83.  |  |
| C116 | DENG et al., CpG oligodeoxynucleotides stimulate protective innate immunity against pulmonary <i>Klebsiella</i> infection. <i>J Immunol.</i> 2004 Oct 15;173(8):5148-55.                          |  |
| C117 | DIWAN et al., Enhancement of immune responses by co-delivery of a CpG oligodeoxynucleotide and tetanus toxoid in biodegradable nanospheres. <i>J Control Release.</i> 2002 Dec 13;85(1-3):247-62. |  |
| C118 | ECKSTEIN, Phosphorothioation of DNA in bacteria. <i>Nat Chem Biol.</i> 2007 Nov;3(11):689-90.   |  |
| C119 | GOLDBERG et al., Beyond danger: unmethylated CpG dinucleotides and the immunopathogenesis of disease. <i>Immunol Lett.</i> 2000 Jul 3;73(1):13-8.   |  |
| C120 | HALPERN et al., Bacterial DNA induces murine interferon-gamma production by stimulation of interleukin-12 and tumor necrosis factor-alpha. <i>Cell Immunol.</i> 1996 Jan 10;167(1):72-8.          |  |
| C121 | HARANDI et al., A protective role of locally administered immunostimulatory CpG oligodeoxynucleotide in a mouse model of genital herpes infection. <i>J Virol.</i> 2003 Jan;77(2):953-62.         |  |
| C122 | HARTMANN et al., CpG DNA and LPS induce distinct patterns of activation in human monocytes. <i>Gene Ther.</i> 1999 May;6(5):893-903.  |  |
| C123 | HARTMANN et al., Delineation of a CpG phosphorothioate oligodeoxynucleotide for activating primate immune responses in vitro and in vivo. <i>J Immunol.</i> 2000 Feb 1;164(3):1617-24.            |  |
| C124 | HARTMANN et al., Identification and functional analysis of tumor-infiltrating plasmacytoid dendritic cells in head and neck cancer. <i>Cancer Res.</i> 2003 Oct 1;63(19):6478-87.                 |  |
| C125 | HARTMANN et al., Mechanism and function of a newly identified CpG DNA motif in human primary B cells. <i>J Immunol.</i> 2000 Jan 15;164(2):944-53.  |  |

|           |                  |
|-----------|------------------|
| EXAMINER: | DATE CONSIDERED: |
|-----------|------------------|

<sup>#</sup> EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

|   |  |  |  |                             |                                   |
|---|--|--|--|-----------------------------|-----------------------------------|
| <b>FORM PTO-1449/A and B (modified PTO/SB/08)</b><br><b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b> |  |  |  | APPLICATION NO.: 10/613,524 | ATTY. DOCKET NO.: C1037.70042US00 |
|   |  |  |  | FILING DATE: July 3, 2003   | CONFIRMATION NO.: 4728            |
|   |  |  |  | APPLICANT: Krieg et al.     |                                   |
|   |  |  |  | Sheet                       | 5                                 |

|  |      |   |  |
|--|------|---|--|
|  | C126 | HARTMANN et al., Rational design of new CpG oligonucleotides that combine B cell activation with high IFN-alpha induction in plasmacytoid dendritic cells. <i>Eur J Immunol.</i> 2003 Jun;33(6):1633-41.  |  |
|  | C127 | HOPKIN et al., Curbing the CpGs of Bacterial and Viral DNA. <i>BioMedNet.</i> 1999 Jun25; Issue 57.   |  |
|  | C128 | HORNER et al., Immunostimulatory DNA is a potent mucosal adjuvant. <i>Cell Immunol.</i> 1998 Nov 25;190(1):77-82.   |  |
|  | C129 | HUANG et al., Induction and regulation of Th1-inducing cytokines by bacterial DNA, lipopolysaccharide, and heat-inactivated bacteria. <i>Infect Immun.</i> 1999 Dec;67(12):6257-63.   |  |
|  | C130 | IHO et al., Oligodeoxynucleotides containing palindrome sequences with internal 5'-CpG-3' act directly on human NK and activated T cells to induce IFN-gamma production in vitro. <i>J Immunol.</i> 1999 Oct 1;163(7):3642-52.  |  |
|  | C131 | INFANTE-DUARTE et al., Th1/Th2 balance in infection. <i>Springer Semin Immunopathol.</i> 1999;21(3):317-38.   |  |
|  | C132 | ISHII et al., Antitumor therapy with bacterial DNA and toxin: complete regression of established tumor induced by liposomal CpG oligodeoxynucleotides plus interleukin-13 cytotoxin. <i>Clin Cancer Res.</i> 2003 Dec 15;9(17):6516-22.   |  |
|  | C133 | JACOBSON et al., Early viral response and on treatment response to CpG 10101 (ACTILON <sup>TM</sup> ), in combination with pegylated interferon and/or ribavirin, in chronic HCV genotype 1 infected patients with prior relapse response. 57 <sup>th</sup> Annual Meeting of American Association for the Study of the Liver Diseases (AASLD). 2006 Oct 30, Boston, Massachusetts; Presented Abstract #96. |  |
|  | C134 | JIANG et al., Enhancing immunogenicity by CpG DNA. <i>Curr Opin Mol Ther.</i> 2003 Apr;5(2):180-5.  |  |
|  | C135 | JIANG et al., Synthetic vaccines: the role of adjuvants in immune targeting. <i>Curr Med Chem.</i> 2003 Aug;10(15):1423-39.   |  |
|  | C136 | KANDIMALLA et al., Secondary structures in CpG oligonucleotides affect immunostimulatory activity. <i>Biochem Biophys Res Commun.</i> 2003 Jul 11;306(4):948-53.  |  |
|  | C137 | KELLAND et al., Of mice and men: values and liabilities of the athymic nude mouse model in anticancer drug development. <i>Eur J Cancer.</i> 2004 Apr;40(6):827-36.   |  |
|  | C138 | KIM et al., Prognostic implication of aberrant promoter hypermethylation of CpG islands in adenocarcinoma of the lung. <i>J Thorac Cardiovasc Surg.</i> 2005 Nov;130(5):1378. Epub 2005 Oct 13.   |  |
|  | C139 | KIM et al., TLR9 Agonist Immunomodulator Treatment of Cutaneous T-cell Lymphomas (CTCL) with CPG7909. <i>Blood.</i> 2004 Nov 16;104(11):Abstract #743.  |  |
|  | C140 | KIMURA et al., Binding of oligoguanosine to scavenger receptors is required for oligonucleotides to augment NK cell activity and induce IFN. <i>J Biochem (Tokyo).</i> 1994 Nov;116(5):991-4.   |  |
|  | C141 | KLINE et al., DNA therapy for asthma. <i>Curr Opin Allergy Clin Immunol.</i> 2002 Feb;2(1):69-73.   |  |
|  | C142 | KLINE et al., Modulation of airway inflammation by CpG oligodeoxynucleotides in a murine model of asthma. <i>J Immunol.</i> 1998 Mar 15;160(6):2555-9.  |  |
|  | C143 | KLINE et al., Treatment of established asthma in a murine model using CpG oligodeoxynucleotides. <i>Am J Physiol Lung Cell Mol Physiol.</i> 2002 Jul;283(1):L170-9.   |  |
|  | C144 | KLINMAN et al., Contribution of CpG motifs to the immunogenicity of DNA vaccines. <i>J Immunol.</i> 1997 Apr 15;158(8):3635-9.  |  |
|  | C145 | KLINMAN et al., CpG motifs present in bacterial DNA rapidly induce lymphocytes to secrete interleukin 6, interleukin 12, and interferon gamma. <i>Proc Natl Acad Sci U S A.</i> 1996 Apr 2;93(7):2879-83.   |  |
|  | C146 | KLINMAN et al., Immunotherapeutic uses of CpG oligodeoxynucleotides. <i>Nat Rev Immunol.</i> 2004 Apr;4(4):249-58.  |  |

|           |                  |
|-----------|------------------|
| EXAMINER: | DATE CONSIDERED: |
|-----------|------------------|

<sup>#</sup> EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

|   |   |    |    |                             |                                   |
|---|---|----|----|-----------------------------|-----------------------------------|
| FORM PTO-1449/A and B (modified PTO/SB/08)    |   |    |    | APPLICATION NO.: 10/613,524 | ATTY. DOCKET NO.: C1037.70042US00 |
| INFORMATION DISCLOSURE STATEMENT BY APPLICANT |   |    |    | FILING DATE: July 3, 2003   | CONFIRMATION NO.: 4728            |
|   |   |    |    | APPLICANT: Krieg et al.     |                                   |
| Sheet   | 6 | of | 12 | GROUP ART UNIT: 1645        | EXAMINER: Oluwatosin A. Ogunbiyi  |

|      |  |
|------|--|
| C147 | KNIPE et al., eds., <i>Fields' Virology</i> . 2001;1:1004-16.  |
| C148 | KNIPE et al., eds., <i>Fields' Virology</i> . 2001;1:1564.   |
| C149 | KOVARIK et al., CpG oligodeoxynucleotides can circumvent the Th2 polarization of neonatal responses to vaccines but may fail to fully redirect Th2 responses established by neonatal priming. <i>J Immunol</i> . 1999 Feb 1;162(3):1611-7.   |
| C150 | KRANZER et al., CpG-oligodeoxynucleotides enhance T-cell receptor-triggered interferon-gamma production and up-regulation of CD69 via induction of antigen-presenting cell-derived interferon type I and interleukin-12. <i>Immunology</i> . 2000 Feb;99(2):170-8.   |
| C151 | KRIEG et al., A role for endogenous retroviral sequences in the regulation of lymphocyte activation. <i>J Immunol</i> . 1989 Oct 15;143(8):2448-51.  |
| C152 | KRIEG et al., Causing a commotion in the blood: immunotherapy progresses from bacteria to bacterial DNA. <i>Immunol Today</i> . 2000 Oct;21(10):521-6.   |
| C153 | KRIEG et al., Chapter 17: Immune Stimulation by Oligonucleotides. In <i>Antisense Drug Tech</i> . 2001;1394:471-515.   |
| C154 | KRIEG et al., Chapter 8: Immune Stimulation by Oligonucleotides. In: <i>Antisense Research and Application</i> . Crooke, Ed. 1998:243-62.  |
| C155 | KRIEG et al., CpG DNA induces sustained IL-12 expression in vivo and resistance to Listeria monocytogenes challenge. <i>J Immunol</i> . 1998 Sep 1;161(5):2428-34.   |
| C156 | KRIEG et al., CpG DNA: a novel immunomodulator. <i>Trends Microbiol</i> . 1999 Feb;7(2):64-5.  |
| C157 | KRIEG et al., CpG motifs in bacterial DNA and their immune effects. <i>Annu Rev Immunol</i> . 2002;20:709-60.  |
| C158 | KRIEG et al., CpG motifs in bacterial DNA trigger direct B-cell activation. <i>Nature</i> . 1995 Apr 6;374(6522):546-9.  |
| C159 | KRIEG et al., Direct immunologic activities of CpG DNA and implications for gene therapy. <i>J Gene Med</i> . 1999 Jan-Feb;1(1):56-63.   |
| C160 | KRIEG et al., How to exclude immunostimulatory and other nonantisense effects of antisense oligonucleotides. <i>Manual of Antisense</i> . 1999:79-89.  |
| C161 | KRIEG et al., Immune effects and therapeutic applications of CpG motifs in bacterial DNA. <i>Immunopharmacology</i> . 2000 Jul 25;48(3):303-5.   |
| C162 | KRIEG et al., Induction of systemic TH1-like immunity in normal volunteers following subcutaneous but not intravenous administration of CPG 7909, a synthetic B-class CpG oligodeoxynucleotide TLR9 agonist. <i>J Immunother</i> . 2004 Nov-Dec;27(6):460-71.  |
| C163 | KRIEG et al., Infection. In: <i>McGraw Hill Book</i> . 1996:242-3.   |
| C164 | KRIEG et al., Leukocyte stimulation by oligodeoxynucleotides. In: <i>Applied Antisense Oligonucleotide Technology</i> . 1998:431-48.   |
| C165 | KRIEG et al., Lymphocyte activation by CpG dinucleotide motifs in prokaryotic DNA. <i>Trends Microbiol</i> . 1996 Feb;4(2):73-6.   |
| C166 | KRIEG et al., Lymphocyte activation mediated by oligodeoxynucleotides or DNA containing novel unmethylated CpG motifs. <i>American College of Rheumatology 58<sup>th</sup> National Scientific Meeting</i> . Minneapolis, Minnesota, October 22, 1994. <i>Abstracts. Arthritis Rheum</i> . 1994 Sep;37(9 Suppl). |
| C167 | KRIEG et al., Mechanism of action of CpG DNA. <i>Curr Top Microbiol Immunol</i> . 2000;247:1-21.   |
| C168 | KRIEG et al., Mechanisms and applications of immune stimulatory CpG oligodeoxynucleotides. <i>Biochim Biophys Acta</i> . 1999 Dec 10;1489(1):107-16.   |

|           |                  |
|-----------|------------------|
| EXAMINER: | DATE CONSIDERED: |
|-----------|------------------|

<sup>#</sup> EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

|  |   |    |    |                             |                                   |
|--|---|----|----|-----------------------------|-----------------------------------|
| <b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b><br><br>FORM PTO-1449/A and B (modified PTO/SB/08) |   |    |    | APPLICATION NO.: 10/613,524 | ATTY. DOCKET NO.: C1037.70042US00 |
|  |   |    |    | FILING DATE: July 3, 2003   | CONFIRMATION NO.: 4728            |
|  |   |    |    | APPLICANT: Krieg et al.     |                                   |
|  |   |    |    | GROUP ART UNIT: 1645        | EXAMINER: Oluwatosin A. Ogunbiyi  |
| Sheet  | 7 | of | 12 |                             |                                   |

|  |      |   |  |
|--|------|---|--|
|  | C169 | KRIEG et al., Modification of antisense phosphodiester oligodeoxynucleotides by a 5' cholestryl moiety increases cellular association and improves efficacy. Proc Natl Acad Sci U S A. 1993 Feb 1;90(3):1048-52.      |  |
|  | C170 | KRIEG et al., Oligodeoxynucleotide modifications determine the magnitude of B cell stimulation by CpG motifs. Antisense Nucleic Acid Drug Dev. 1996 Summer;6(2):133-9.  |  |
|  | C171 | KRIEG et al., P-chirality-dependent immune activation by phosphorothioate CpG oligodeoxynucleotides. Oligonucleotides. 2003;13(6):491-9.  |  |
|  | C172 | KRIEG et al., Phosphorothioate oligodeoxynucleotides: antisense or anti-protein? Antisense Res Dev. 1995 Winter;5(4):241.   |  |
|  | C173 | KRIEG et al., Rescue of B cells from apoptosis by immune stimulatory CpG DNA. Springer Semin Immunopathol. 2000;22(1-2):55-61.  |  |
|  | C174 | KRIEG et al., Sequence motifs in adenoviral DNA block immune activation by stimulatory CpG motifs. Proc Natl Acad Sci U S A. 1998 Oct 13;95(21):12631-6.  |  |
|  | C175 | KRIEG et al., The role of CpG dinucleotides in DNA vaccines. Trends Microbiol. 1998 Jan;6(1):23-7.  |  |
|  | C176 | KRIEG et al., Unmethylated CpG DNA protects mice from lethal listeria monocytogenes challenge. Vaccines. 1997; 97:77-9.   |  |
|  | C177 | KRIEG, An innate immune defense mechanism based on the recognition of CpG motifs in microbial DNA. J Lab Clin Med. 1996 Aug;128(2):128-33.  |  |
|  | C178 | KRIEG, Antiinfective applications of toll-like receptor 9 agonists. Proc Am Thorac Soc. 2007 Jul;4(3):289-94.   |  |
|  | C179 | KRIEG, Chapter 7: CpG oligonucleotides as immune adjuvants. Ernst Schering Research Found Workshop 2001; 30:105-18.   |  |
|  | C180 | KRIEG, CpG DNA: a pathogenic factor in systemic lupus erythematosus? J Clin Immunol. 1995 Nov;15(6):284-92.   |  |
|  | C181 | KRIEG, Now I know my CpGs. Trends Microbiol. 2001 Jun;9(6):249-52.  |  |
|  | C182 | KRIEG, Signal transduction induced by immunostimulatory CpG DNA. Springer Semin Immunopathol. 2000;22(1-2):97-105.  |  |
|  | C183 | KRIEG, Therapeutic potential of Toll-like receptor 9 activation. Nat Rev Drug Discov. 2006 Jun;5(6):471-84.   |  |
|  | C184 | KURAMOTO et al., Changes of host cell infiltration into Meth A fibrosarcoma tumor during the course of regression induced by injections of a BCG nucleic acid fraction. Int J Immunopharmacol. 1992 Jul;14(5):773-82. |  |
|  | C185 | KURAMOTO et al., In situ infiltration of natural killer-like cells induced by intradermal injection of the nucleic acid fraction from BCG. Microbiol Immunol. 1989;33(11):929-40.                                     |  |
|  | C186 | KURAMOTO et al., Oligonucleotide sequences required for natural killer cell activation. Jpn J Cancer Res. 1992 Nov;83(11):1128-31.  |  |
|  | C187 | LEE et al., Effects of a hexameric deoxyriboguanosine run conjugation into CpG oligodeoxynucleotides on their immunostimulatory potentials. J Immunol. 2000 Oct 1;165(7):3631-9                                       |  |
|  | C188 | LI et al., Effective induction of CD8+ T-cell response using CpG oligodeoxynucleotides and HER-2/neu-derived peptide co-encapsulated in liposomes. Vaccine. 2003 Jul 4;21(23):3319-29.                                |  |
|  | C189 | LIPFORD et al., Immunostimulatory DNA: sequence-dependent production of potentially harmful or useful cytokines. Eur J Immunol. 1997 Dec;27(12):3420-6.   |  |
|  | C190 | LIPFORD et al., Bacterial DNA as immune cell activator. Trends Microbiol. 1998 Dec;6(12):496-500.   |  |
|  | C191 | MAJOR et al., Chapter 34 Hepatitis C Viruses. in Fields' Virology. 2001; 1:1127-61  |  |

|           |                  |
|-----------|------------------|
| EXAMINER: | DATE CONSIDERED: |
|-----------|------------------|

<sup>#</sup> EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

|   |   |    |    |                             |                                   |
|---|---|----|----|-----------------------------|-----------------------------------|
| FORM PTO-1449/A and B (modified PTO/SB/08)    |   |    |    | APPLICATION NO.: 10/613,524 | ATTY. DOCKET NO.: C1037.70042US00 |
| INFORMATION DISCLOSURE STATEMENT BY APPLICANT |   |    |    | FILING DATE: July 3, 2003   | CONFIRMATION NO.: 4728            |
|   |   |    |    | APPLICANT: Krieg et al.     |                                   |
| Sheet   | 8 | of | 12 | GROUP ART UNIT: 1645        | EXAMINER: Oluwatosin A. Ogunbiyi  |

|      |  |  |
|------|--|--|
| C192 | MARSHALL et al., Identification of a novel CpG DNA class and motif that optimally stimulate B cell and plasmacytoid dendritic cell functions. <i>J Leukoc Biol.</i> 2003 Jun;73(6):781-92.   |  |
| C193 | MARTIN-OROZCO et al., Enhancement of antigen-presenting cell surface molecules involved in cognate interactions by immunostimulatory DNA sequences. <i>Int Immunol.</i> 1999 Jul;11(7):1111-8.   |  |
| C194 | MASIHI et al., Fighting infection using immunomodulatory agents. <i>Expert Opin Biol Ther.</i> 2001 Jul;1(4):641-53.   |  |
| C195 | McCLUSKIE et al., Route and method of delivery of DNA vaccine influence immune responses in mice and non-human primates. <i>Mol Med.</i> 1999 May;5(5):287-300.  |  |
| C196 | McCLUSKIE et al., The role of CpG in DNA vaccines. <i>Springer Semin Immunopathol.</i> 2000;22(1-2):125-32.  |  |
| C197 | McCLUSKIE et al., The use of CpG DNA as a mucosal vaccine adjuvant. <i>Curr Opin Investig Drugs.</i> 2001 Jan;2(1):35-9.   |  |
| C198 | McHUTCHISON et al., Early clinical results with CpG 10101, a new investigational antiviral TLR9 agonist being developed for treatment of subjects chronically infected with hepatitis C virus. 12 <sup>th</sup> International Symposium on Viral Hepatitis and Liver Disease (ISVHLD). 2006 July 3, Paris, France; Presented Abstract #O105. |  |
| C199 | McHUTCHISON et al., Early viral response to CpG 10101, in combination with pegylated interferon and/or ribavirin, in chronic HCV genotype 1 infected patients with prior relapse response. 41 <sup>st</sup> Annual Meeting of European Association for the Study of the Liver (EASL). 2006 April 26-30, Vienna, Austria; Submitted Abstract. |  |
| C200 | McHUTCHISON et al., Final results of a multi-center phase 1B, randomized, placebo-controlled, dose-escalation trial of CpG 10101 in patients with chronic hepatitis C virus. 41 <sup>st</sup> Annual Meeting of European Association for the Study of the Liver (EASL). 2006 April 30, Vienna, Austria; Presented Abstract #111.             |  |
| C201 | MESSINA et al., The influence of DNA structure on the in vitro stimulation of murine lymphocytes by natural and synthetic polynucleotide antigens. <i>Cell Immunol.</i> 1993 Mar;147(1):148-57.  |  |
| C202 | NORMAN et al., Liposome-mediated, nonviral gene transfer induces a systemic inflammatory response which can exacerbate pre-existing inflammation. <i>Gene Ther.</i> 2000;7:1425-30.  |  |
| C203 | PAYETTE et al., History of vaccines and positioning of current trends. <i>Curr Drug Targets Infect Disord.</i> 2001 Nov;1(3):241-7.  |  |
| C204 | PETERSON et al., Integrating pharmacology and in vivo cancer models in preclinical and clinical drug development. <i>Eur J Cancer.</i> 2004 Apr;40(6):837-44.  |  |
| C205 | PISETSKY et al., Stimulation of in vitro proliferation of murine lymphocytes by synthetic oligodeoxynucleotides. <i>Mol Biol Rep.</i> 1993 Oct;18(3):217-21.   |  |
| C206 | PISETSKY et al., The influence of base sequence on the immunological properties of defined oligonucleotides. <i>Immunopharmacology.</i> 1998 Nov;40(3):199-208.  |  |
| C207 | PISETSKY, Immunologic consequences of nucleic acid therapy. <i>Antisense Res Dev.</i> 1995 Fall;5(3):219-25.   |  |
| C208 | PISETSKY, The influence of base sequence on the immunostimulatory properties of DNA. <i>Immunol Res.</i> 1999;19(1):35-46.   |  |
| C209 | POLANCZYK et al., Immunostimulatory effects of DNA and CpG motifs. <i>Cent Eur J of Immunol.</i> 2000;25(3):160-6.   |  |
| C210 | RANKIN et al., CpG motif identification for veterinary and laboratory species demonstrates that sequence recognition is highly conserved. <i>Antisense Nucleic Acid Drug Dev.</i> 2001 Oct;11(5):333-40.   |  |

|           |                  |
|-----------|------------------|
| EXAMINER: | DATE CONSIDERED: |
|-----------|------------------|

<sup>#</sup> EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

|   |   |    |    |                             |                                   |
|---|---|----|----|-----------------------------|-----------------------------------|
| FORM PTO-1449/A and B (modified PTO/SB/08)    |   |    |    | APPLICATION NO.: 10/613,524 | ATTY. DOCKET NO.: C1037.70042US00 |
| INFORMATION DISCLOSURE STATEMENT BY APPLICANT |   |    |    | FILING DATE: July 3, 2003   | CONFIRMATION NO.: 4728            |
|   |   |    |    | APPLICANT: Krieg et al.     |                                   |
|   |   |    |    | GROUP ART UNIT: 1645        |                                   |
| Sheet   | 9 | of | 12 |                             |                                   |

|      |   |  |
|------|---|--|
| C211 | READETT et al., PF-3512676 (CPG7909) a Toll-like receptor 9 agonist – status of development for non-small cell lung cancer (NSCLC). Abstract PD3-1-6. Pfizer. 24 Aug. 2007. Poster.   |  |
| C212 | RODRIGUEZ et al., Immunostimulatory PyNTTTGT oligodeoxynucleotides: structural properties and refinement of the active motif. Oligonucleotides. 2006 Fall;16(3):275-85.   |  |
| C213 | ROMAN et al., Immunostimulatory DNA sequences function as T helper-1-promoting adjuvants. Nat Med. 1997 Aug;3(8):849-54.  |  |
| C214 | ROTHENFUSSER et al., Recent advances in immunostimulatory CpG oligonucleotides. Curr Opin Mol Ther. 2003 Apr;5(2):98-106.   |  |
| C215 | RUDGINSKY et al., Antitumor activity of cationic lipid complexed with immunostimulatory DNA. Mol Ther. 2001 Oct;4(4):347-55.  |  |
| C216 | RYNKIEWICZ et al., Marked enhancement of antibody response to anthrax vaccine adsorbed with CPG 7909 in healthy volunteers. 45 <sup>th</sup> Intersci. Conf. Antimicrob. Agents Chemother. 2005 Sep. 21-24; New Orleans, Louisiana. Meeting Poster. |  |
| C217 | SAIJO et al., What are the reasons for negative phase III trials of molecular-target-based drugs? Cancer Sci. 2004 Oct;95(10):772-6.  |  |
| C218 | SAKAO et al., IL-18-deficient mice are resistant to endotoxin-induced liver injury but highly susceptible to endotoxin shock. Int Immunol. 1999 Mar;11(3):471-80.   |  |
| C219 | SATO et al., Immunostimulatory DNA sequences necessary for effective intradermal gene immunization. Science. 1996 Jul 19;273(5273):352-4.   |  |
| C220 | SATOH et al., Morphological and immunohistochemical characteristics of the heterogeneous prostate-like glands (paraurethral gland) seen in female Brown-Norway rats. Toxicol Pathol. 2001 Mar-Apr;29(2):237-41.                                     |  |
| C221 | SCHELLER et al., CpG oligodeoxynucleotides activate HIV replication in latently infected human T cells. J Biol Chem. 2004 May 21;279(21):21897-902. Epub 2004 Mar 11.   |  |
| C222 | SCHEULE, The role of CpG motifs in immunostimulation and gene therapy. Adv Drug Deliv Rev. 2000 Nov 15;44(2-3):119-34.  |  |
| C223 | SCHUH et al., Trials, tribulations, and trends in tumor modeling in mice. Toxicol Pathol. 2004 Mar-Apr;32 Suppl 1:53-66.  |  |
| C224 | SCHWARTZ et al., Bacterial DNA or oligonucleotides containing unmethylated CpG motifs can minimize lipopolysaccharide-induced inflammation in the lower respiratory tract through an IL-12-dependent pathway. J Immunol. 1999 Jul 1;163(1):224-31.  |  |
| C225 | SCHWARZ et al., Role of Toll-like receptors in costimulating cytotoxic T cell responses. Eur J Immunol. 2003 Jun;33(6):1465-70.   |  |
| C226 | SESTER et al., Phosphorothioate backbone modification modulates macrophage activation by CpG DNA. J Immunol. 2000 Oct 15;165(8):4165-73.  |  |
| C227 | SFONDRINI et al., Prevention of spontaneous mammary adenocarcinoma in HER-2/neu transgenic mice by foreign DNA. FASEB J. 2002 Nov;16(13):1749-54.   |  |
| C228 | SHALABY, Development of oral vaccines to stimulate mucosal and systemic immunity: barriers and novel strategies. Clin Immunol Immunopathol. 1995 Feb;74(2):127-34.  |  |
| C229 | SHAO et al., CpG-containing oligodeoxynucleotide 1826 converts the weak uveitogenic rat interphotoreceptor retinoid-binding protein peptide 1181-1191 into a strong uveitogen. J Immunol. 2003 Nov 1;171(9):4780-5.                                 |  |
| C230 | SIEGRIST et al., Co-administration of CpG oligonucleotides enhances the late affinity maturation process of human anti-hepatitis B vaccine response. Vaccine. 2004 Dec 16;23(5):615-22.   |  |

|           |                  |
|-----------|------------------|
| EXAMINER: | DATE CONSIDERED: |
|-----------|------------------|

<sup>#</sup> EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

|  |    |    |    |                             |                                   |
|--|----|----|----|-----------------------------|-----------------------------------|
| <b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b><br><br>FORM PTO-1449/A and B (modified PTO/SB/08) |    |    |    | APPLICATION NO.: 10/613,524 | ATTY. DOCKET NO.: C1037.70042US00 |
|  |    |    |    | FILING DATE: July 3, 2003   | CONFIRMATION NO.: 4728            |
|  |    |    |    | APPLICANT: Krieg et al.     |                                   |
|  |    |    |    | GROUP ART UNIT: 1645        | EXAMINER: Oluwatosin A. Ogunbiyi  |
| Sheet  | 10 | of | 12 |                             |                                   |

|  |      |  |   |
|--|------|--|---|
|  | C231 | SONEHARA et al., Hexamer palindromic oligonucleotides with 5'-CG-3' motif(s) induce production of interferon. <i>J Interferon Cytokine Res.</i> 1996 Oct;16(10):799-803.   |   |
|  | C232 | SPARWASSER et al., Bacterial DNA causes septic shock. <i>Nature.</i> 1997 Mar 27;386(6623):336-7.  |   |
|  | C233 | SPARWASSER et al., Immunostimulatory CpG-oligodeoxynucleotides cause extramedullary murine hemopoiesis. <i>J Immunol.</i> 1999 Feb 15;162(4):2368-74.  |   |
|  | C234 | SPARWASSER et al., Macrophages sense pathogens via DNA motifs: induction of tumor necrosis factor-alpha-mediated shock. <i>Eur J Immunol.</i> 1997 Jul;27(7):1671-9.   |   |
|  | C235 | STEIN et al., Non-antisense effects of oligodeoxynucleotides. <i>Antisense Technology.</i> 1997; Ch.11:241-64.   |   |
|  | C236 | STEIN et al., Problems in interpretation of data derived from in vitro and in vivo use of antisense oligodeoxynucleotides. <i>Antisense Res Dev.</i> 1994 Summer;4(2):67-9.  |   |
|  | C237 | STOREY et al., Anti-sense phosphorothioate oligonucleotides have both specific and non-specific effects on cells containing human papillomavirus type 16. <i>Nucleic Acids Res.</i> 1991 Aug 11;19(15):4109-14.                                |   |
|  | C238 | SUN et al., Multiple effects of immunostimulatory DNA on T cells and the role of type I interferons. <i>Springer Semin Immunopathol.</i> 2000;22(1-2):77-84.   |   |
|  | C239 | SUN et al., Type I interferon-mediated stimulation of T cells by CpG DNA. <i>J Exp Med.</i> 1998 Dec 21;188(12):2335-42.   |   |
|  | C240 | THREADGILL et al., Mitogenic synthetic polynucleotides suppress the antibody response to a bacterial polysaccharide. <i>Vaccine.</i> 1998 Jan;16(1):76-82.   |   |
|  | C241 | TOKUNAGA et al., Synthetic oligonucleotides with particular base sequences from the cDNA encoding proteins of <i>Mycobacterium bovis</i> BCG induce interferons and activate natural killer cells. <i>Microbiol Immunol.</i> 1992;36(1):55-66. |   |
|  | C242 | TOKUNAGA, Response of the organism to DNA – With a focus on immunostimulatory DNA. <i>Kansen Ensho Meneki.</i> 2001 Autumn; 31(3): 1-12. Japanese.   | Y |
|  | C243 | TZAO et al., 5'CpG island hypermethylation and aberrant transcript splicing both contribute to the inactivation of the FHIT gene in resected non-small cell lung cancer. <i>Eur J Cancer.</i> 2004 Sep;40(14):2175-83.                         |   |
|  | C244 | UHLMANN et al., Recent advances in the development of immunostimulatory oligonucleotides. <i>Curr Opin Drug Discov Devel.</i> 2003 Mar;6(2):204-17.  |   |
|  | C245 | VERTHELGYI et al., Human peripheral blood cells differentially recognize and respond to two distinct CPG motifs. <i>J Immunol.</i> 2001 Feb 15;166(4):2372-7.  |   |
|  | C246 | VOLLMER et al., Characterization of three CpG oligodeoxynucleotide classes with distinct immunostimulatory activities. <i>Eur J Immunol.</i> 2004 Jan;34(1):251-62.  |   |
|  | C247 | VOLLMER et al., Highly immunostimulatory CpG-free oligodeoxynucleotides for activation of human leukocytes. <i>Antisense Nucleic Acid Drug Dev.</i> 2002 Jun;12(3):165-75.   |   |
|  | C248 | VOLLMER et al., Impact of modifications of heterocyclic bases in CpG dinucleotides on their immune-modulatory activity. <i>J Leukoc Biol.</i> 2004 Sep;76(3):585-93. Epub 2004 Jun 24.   |   |
|  | C249 | VOLLMER et al., Modulation of CpG oligodeoxynucleotide-mediated immune stimulation by locked nucleic acid (LNA). <i>Oligonucleotides.</i> 2004 Spring;14(1):23-31.   |   |
|  | C250 | VOLLMER, TLR9 in health and disease. <i>Int Rev Immunol.</i> 2006 May-Aug;25(3-4):155-81.  |   |
|  | C251 | WAGNER, Interactions between bacterial CpG-DNA and TLR9 bridge innate and adaptive immunity. <i>Curr Opin Microbiol.</i> 2002 Feb;5(1):62-9.   |   |

|           |                  |
|-----------|------------------|
| EXAMINER: | DATE CONSIDERED: |
|-----------|------------------|

<sup>#</sup> EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

|  |    |    |    |                             |                                   |
|--|----|----|----|-----------------------------|-----------------------------------|
| FORM PTO-1449/A and B (modified PTO/SB/08)<br><b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b> |    |    |    | APPLICATION NO.: 10/613,524 | ATTY. DOCKET NO.: C1037.70042US00 |
|  |    |    |    | FILING DATE: July 3, 2003   | CONFIRMATION NO.: 4728            |
|  |    |    |    | APPLICANT: Krieg et al.     |                                   |
|  |    |    |    | GROUP ART UNIT: 1645        | EXAMINER: Oluwatosin A. Ogunbiyi  |
| Sheet  | 11 | of | 12 |                             |                                   |

|  |      |   |   |
|--|------|---|---|
|  | C252 | WANG et al., Phosphorothioation of DNA in bacteria by dnd genes. <i>Nat Chem Biol.</i> 2007 Nov;3(11):709-10. Epub 2007 Oct 14. Supplementary information, 12 pages.  |   |
|  | C253 | WANG et al., T-cell-directed cancer vaccines: the melanoma model. <i>Expert Opin Biol Ther.</i> 2001 Mar;1(2):277-90.   |   |
|  | C254 | WEERATNA et al., CpG DNA induces stronger immune responses with less toxicity than other adjuvants. <i>Vaccine.</i> 2000 Mar 6;18(17):1755-62.  |   |
|  | C255 | WHITMORE et al., LPD lipopolyplex initiates a potent cytokine response and inhibits tumor growth. <i>Gene Ther.</i> 1999;6:1867-75.   |   |
|  | C256 | WHITMORE et al., Systemic administration of LPD prepared with CpG oligonucleotides inhibits the growth of established pulmonary metastases by stimulating innate and acquired antitumor immune responses. <i>Canc Immun Immunother.</i> 2001;50:503-14. |   |
|  | C257 | WOHLLEBEN et al., Atopic disorders: a vaccine around the corner? <i>Trends Immunol.</i> 2001 Nov;22(11):618-26.   |   |
|  | C258 | YAMADA et al., Effect of suppressive DNA on CpG-induced immune activation. <i>J Immunol.</i> 2002 Nov 15;169(10):5590-4.  |   |
|  | C259 | YAMAMOTO et al., [Commemorative lecture of receiving Imamura Memorial Prize. II. Mode of action of oligonucleotide fraction extracted from <i>Mycobacterium bovis BCG</i> ] <i>Kekkaku.</i> 1994 Sep;69(9):571-4. Japanese.                             | Y |
|  | C260 | YAMAMOTO et al., Ability of oligonucleotides with certain palindromes to induce interferon production and augment natural killer cell activity is associated with their base length. <i>Antisense Res Dev.</i> 1994 Summer;4(2):119-22.                 |   |
|  | C261 | YAMAMOTO et al., Lipofection of synthetic oligodeoxyribonucleotide having a palindromic sequence of AACGTT to murine splenocytes enhances interferon production and natural killer activity. <i>Microbiol Immunol.</i> 1994;38(10):831-6.               |   |
|  | C262 | YAMAMOTO et al., Synthetic oligonucleotides with certain palindromes stimulate interferon production of human peripheral blood lymphocytes in vitro. <i>Jpn J Cancer Res.</i> 1994 Aug;85(8):775-9.   |   |
|  | C263 | YAMAMOTO et al., Unique palindromic sequences in synthetic oligonucleotides are required to induce IFN [correction of INF] and augment IFN-mediated [correction of INF] natural killer activity. <i>J Immunol.</i> 1992 Jun 15;148(12):4072-6.          |   |
|  | C264 | YI et al., CpG oligodeoxyribonucleotides rescue mature spleen B cells from spontaneous apoptosis and promote cell cycle entry. <i>J Immunol.</i> 1998 Jun 15;160(12):5898-906.  |   |
|  | C265 | YI et al., Rapid induction of mitogen-activated protein kinases by immune stimulatory CpG DNA. <i>J Immunol.</i> 1998 Nov 1;161(9):4493-7.  |   |
|  | C266 | YI et al., IFN-gamma promotes IL-6 and IgM secretion in response to CpG motifs in bacterial DNA and oligodeoxynucleotides. <i>J Immunol.</i> 1996 Jan 15;156(2):558-64.   |   |
|  | C267 | YI et al., Rapid immune activation by CpG motifs in bacterial DNA. Systemic induction of IL-6 transcription through an antioxidant-sensitive pathway. <i>J Immunol.</i> 1996 Dec 15;157(12):5394-402.   |   |
|  | C268 | YU et al., Potent CpG oligonucleotides containing phosphodiester linkages: in vitro and in vivo immunostimulatory properties. <i>Biochem Biophys Res Commun.</i> 2002 Sep 13;297(1):83-90.  |   |
|  | C269 | ZAITSEVA et al., Interferon gamma and interleukin 6 modulate the susceptibility of macrophages to human immunodeficiency virus type 1 infection. <i>Blood.</i> 2000 Nov 1;96(9):3109-17.  |   |
|  | C270 | ZHANG et al., Antisense oligonucleotide inhibition of hepatitis C virus (HCV) gene expression in livers of mice infected with an HCV-vaccinia virus recombinant. <i>Antimicrob Agents Chemother.</i> 1999 Feb;43(2):347-53.                             |   |

|           |                  |
|-----------|------------------|
| EXAMINER: | DATE CONSIDERED: |
|-----------|------------------|

<sup>#</sup> EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

|  |    |    |    |                             |                                   |
|--|----|----|----|-----------------------------|-----------------------------------|
| FORM PTO-1449/A and B (modified PTO/SB/08) |    |    |    | APPLICATION NO.: 10/613,524 | ATTY. DOCKET NO.: C1037.70042US00 |
|  |    |    |    | FILING DATE: July 3, 2003   | CONFIRMATION NO.: 4728            |
|  |    |    |    | APPLICANT: Krieg et al.     |                                   |
| Sheet                                      | 12 | of | 12 | GROUP ART UNIT: 1645        | EXAMINER: Oluwatosin A. Ogunbiyi  |

|  |      |  |  |
|--|------|--|--|
|  | C271 | ZHAO et al., Pattern and kinetics of cytokine production following administration of phosphorothioate oligonucleotides in mice. <i>Antisense Nucleic Acid Drug Dev.</i> 1997 Oct;7(5):495-502. |  |
|  | C272 | ZIPS et al., New anticancer agents: in vitro and in vivo evaluation. <i>In Vivo.</i> 2005 Jan-Feb;19(1):1-7.   |  |

[NOTE – No copies of U.S. patents, published U.S. patent applications, or pending, unpublished patent applications stored in the USPTO's Image File Wrapper (IFW) system, are included. See 37 CFR §1.98 and 1287OG163. Copies of all other patent(s), publication(s), unpublished, pending U.S. patent applications, or other information listed are provided as required by 37 CFR §1.98 unless 1) such copies were provided in an IDS in an earlier application that complies with 37 CFR §1.98, and 2) the earlier application is relied upon for an earlier filing date under 35 U.S.C. §120.]

|           |                  |
|-----------|------------------|
| EXAMINER: | DATE CONSIDERED: |
|-----------|------------------|

<sup>#</sup> EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.